

What is claimed is:

1. A method of identifying genes that are over-expressed in adipose tissue as compared to non-adipose tissue comprising performing differential gene expression analysis between the white adipose tissue (WAT) or stromal vascular tissue (SVT) from any two different mice selected from the group consisting of wild-type, HMGI-C $-/-$, ob/ob, and HMGI-C $-/-$ ob/ob genotype mice.
2. The method of claim 1, wherein the adipose tissue is adipocytes.
3. The method of claim 1, wherein the adipose tissue is preadipocytes.
4. The method of claim 1, wherein the differential gene expression analysis is performed between the WAT of wild-type mice and the WAT of HMGI-C $-/-$ mice.
5. The method of claim 1, wherein the differential gene expression is performed between the WAT of HMGI-C $-/-$ mice and the WAT of double homozygous ob/ob, HMGI-C $-/-$ mice.
6. The method of claim 1, wherein the differential gene expression analysis is performed between the WAT of ob/ob mice and the WAT of HMGI-C $-/-$ mice.
7. The method of claim 1, wherein the differential gene expression analysis is performed between the WAT of wild-type mice and the SVT of wild-type mice.
8. The method of any one of claims 1-7 wherein the differential gene expression analysis is performed using an Affymetrix GeneChip® system.
9. The method of claim 8, wherein the Affymetrix GeneChip® system utilizes the MG-U74 chip.
10. A nucleotide sequence identified by the method of any one of claims 1-9.
11. The nucleotide sequence of claim 10 having the sequence set forth in any one of SEQ.ID.NO. 1-279.
12. An isolated polynucleotide comprising
 - a) a nucleotide sequence of any one of SEQ ID NOs: 86, 87, 93, 96, 115, 116, 117, 135, 145, 148, 151, 160, 172, 179, 180, 191, 192, 201, 223, 224, 229, 236, 246, 255, 256, 263, 264, 267, 268, 276 or 277, or any one of SEQ ID NOs: 84, 85, 88, 97, 98, 99, 100, 105, 106, 107, 108, 109, 110, 111, 112, 115, 116, 117, 122, 123, 124, 125, 128, 129, 130, 131, 132, 133, 138, 139, 149, 150, 175, 176, 177, 178, 181, 182, 183, 184, 187, 188, 189, 190,

199, 200, 210, 211, 214, 215, 216, 217, 218, 219, 220, 221, 222, 227, 228, 232, 233, 239, 240, 241, 242, 243, 244, 245, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 259, 260, 261, 262, 268, 272 or 273;

b) a nucleotide sequence coding for the same polypeptide as that encoded by the nucleic acid of part a);

c) a nucleotide sequence that has at least 90% identity over the entire coding region to the nucleotide sequence of part a); or

c) a nucleotide sequence complementary to the isolated nucleic acid molecule.

13. The isolated polynucleotide of claim 12 comprising the nucleotide sequence of any one of SEQ ID NOs: 86, 87, 93, 96, 115, 116, 117, 135, 145, 148, 151, 160, 172, 179, 180, 191, 192, 201, 223, 224, 229, 236, 246, 255, 256, 263, 264, 267, 268, 276 or 277.

14. The isolated polynucleotide of claim 12 or 13 comprising the nucleotide sequence of any one of SEQ ID NOs: 84, 85, 88, 97, 98, 99, 100, 105, 106, 107, 108, 109, 110, 111, 112, 115, 116, 117, 122, 123, 124, 125, 128, 129, 130, 131, 132, 133, 138, 139, 149, 150, 175, 176, 177, 178, 181, 182, 183, 184, 187, 188, 189, 190, 199, 200, 210, 211, 214, 215, 216, 217, 218, 219, 220, 221, 222, 227, 228, 232, 233, 239, 240, 241, 242, 243, 244, 245, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 259, 260, 261, 262, 268, 272 or 273.

15. An isolated polynucleotide of claim 12 comprising a nucleotide sequence coding for the same polypeptide as that encoded by any one of SEQ ID NOs: 86, 87, 93, 96, 115, 116, 117, 135, 145, 148, 151, 160, 172, 179, 180, 191, 192, 201, 223, 224, 229, 236, 246, 255, 256, 263, 264, 267, 268, 276 or 277, or any one of SEQ ID NOs: 84, 85, 88, 97, 98, 99, 100, 105, 106, 107, 108, 109, 110, 111, 112, 115, 116, 117, 122, 123, 124, 125, 128, 129, 130, 131, 132, 133, 138, 139, 149, 150, 175, 176, 177, 178, 181, 182, 183, 184, 187, 188, 189, 190, 199, 200, 210, 211, 214, 215, 216, 217, 218, 219, 220, 221, 222, 227, 228, 232, 233, 239, 240, 241, 242, 243, 244, 245, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 259, 260, 261, 262, 268, 272 or 273.

16. The polynucleotide of any one of claims 12-15 which is DNA or RNA.

17. The isolated polynucleotide of any one of claims 12-16, further comprising an expression system that is capable of transcribing the nucleic acid sequence and producing the corresponding amino acid sequence.

18. A host cell comprising a polynucleotide sequence of as defined in any one of claims 12-18.

19. The host cell of claim 18, wherein the polynucleotide sequence is stably incorporated into the genome of the host cell.

20. A process for producing a polypeptide comprising culturing a host of claim 18 or 19 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.

21. A process for producing a cell which produces a polypeptide comprising transforming or transfecting a host cell with the polynucleotide of claim 6 such that the host cell, under appropriate culture conditions, produces the polypeptide.

22. A polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid encoded by any one of SEQ ID NOs: 86, 87, 93, 96, 115, 116, 117, 135, 145, 148, 151, 160, 172, 179, 180, 191, 192, 201, 223, 224, 229, 236, 246, 255, 256, 263, 264, 267, 268, 276 or 277, or any one of SEQ ID NOs: 84, 85, 88, 97, 98, 99, 100, 105, 106, 107, 108, 109, 110, 111, 112, 115, 116, 117, 122, 123, 124, 125, 128, 129, 130, 131, 132, 133, 138, 139, 149, 150, 175, 176, 177, 178, 181, 182, 183, 184, 187, 188, 189, 190, 199, 200, 210, 211, 214, 215, 216, 217, 218, 219, 220, 221, 222, 227, 228, 232, 233, 239, 240, 241, 242, 243, 244, 245, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 259, 260, 261, 262, 268, 272 or 273.

23. The polypeptide of claim 22 which comprises the amino acid encoded by any one of SEQ ID NOs: 86, 87, 93, 96, 115, 116, 117, 135, 145, 148, 151, 160, 172, 179, 180, 191, 192, 201, 223, 224, 229, 236, 246, 255, 256, 263, 264, 267, 268, 276 or 277.

24. A monoclonal antibody immunospecific for the polypeptide of claim 22 or 23.

25. A method for the treatment of a subject in need of enhanced activity or expression of the polypeptide which is at least 90% identical to the amino acid encoded by any one of SEQ.ID.NO. 1 to 279 comprising:

(a) administering to the subject a therapeutically effective amount of an agonist to the polypeptide; and/or (b) administering to the subject an isolated polynucleotide comprising a nucleotide sequence, or a nucleotide sequence complementary to said nucleotide sequence in a form so as to effect production of such polypeptide in vivo;

and/or (c) administering to the subject a therapeutically effective amount of the polypeptide.

26. A method for the treatment of a subject in need of decreased activity or expression of the polypeptide which is at least 90% identical to the amino acid encoded by any one of SEQ.ID.NO. 1 to 279 comprising:

(a) administering to the subject a therapeutically effective amount of an antagonist to said polypeptide; and/or (b) administering to the subject a nucleic acid molecule that inhibits the expression of the nucleotide sequence encoding said polypeptide; and/or (c) administering to the subject a therapeutically effective amount of a polypeptide that competes with said polypeptide for its ligand, substrate, or receptor.

27. A process for diagnosing a susceptibility to obesity or diabetes in a subject related to expression or activity of the polypeptide which comprises the amino acid encoded by any one of SEQ.ID.NO. 1 to 279 in a subject comprising: (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said polypeptide in the genome of said subject; and/or (b) analyzing for the presence or amount of the polypeptide expression in a sample derived from said subject.

28. A method for identifying compounds which antagonize or agonize the polypeptide which is at least 90% identical to the amino acid encoded by any one of SEQ.ID.NO. 1 to 279 comprising:

(a) contacting a candidate compound with cells which express the polypeptide (or cell membrane expressing the polypeptide or a fragment thereof bound to a solid matrix) or respond to the polypeptide; and

(b) observing the binding, or stimulation or inhibition of a functional response; or comparing the ability of the cells (or cell membrane) which were contacted with the candidate compound(s) with the same cells which were not so contacted for polypeptide activity.

29. An agonist identified by the method of claim 28.

30. An antagonist identified by the method of claim 28.

31. A recombinant host cell produced by a method of claim 21 or a membrane thereof expressing a polypeptide.

32. A method for screening for modulators of a target protein, wherein the target protein is encoded by a nucleotide having the sequence set forth in any one of SEQ.ID.NO. 1 to 279 or has 90% amino acid identity to such protein as measured using a sequence comparison algorithm, the method comprising the steps of

- a) contacting the target protein with a candidate agent at a first concentration and determining a level of activity of the target protein; and
- b) contacting the target protein with a candidate agent at a second concentration and determining a level of activity of the target protein; wherein a difference between the level of activity of the target protein contacted with the first concentration of the candidate agent and the level of activity of the target protein contacted with the second concentration of the candidate agent indicates that the candidate agent modulates the activity of the target protein.

33. The method of claim 32, wherein the screening occurs in a multi-well plate as part of a high-throughput screen.

34. The method of any one of claims 32-33, wherein the target protein has greater than 95% amino acid sequence identity to the protein encoded by a nucleotide having a sequence set forth in any one of SEQ.ID.NO: 1-279 as measured using a sequence comparison algorithm.

35. The method of any one of claims 32-34, wherein the target protein comprises an amino acid sequence of encoded by a nucleotide having a sequence set forth in any one of SEQ.ID.NO: 1-279.

36. The method of claim 35, wherein the target protein has been isolated from an endogenous source.

37. The method of claim 35, wherein the target protein has been produced recombinantly.

38. The method of any one of claims 32-37, wherein said first concentration or aid second concentration of the candidate agent is zero or at a level below detection.

39. The method of any one of claims 32-38, wherein the candidate agent is an agonist.

40. The method of any one of claims 32-38, wherein the candidate agent is an antagonist.

41. The method of any one of claims 32-38, wherein the candidate agent binds to the target protein.

42. The method of any one of claims 32-38, wherein the target protein is contacted with the candidate agent in vivo.

43. The method of any one of claims 32-38, wherein the target protein is contacted with the candidate agent in vitro.

44. The method of any one of claims 32-38, wherein the candidate agent is labeled.

45. A bioassay for identifying compounds which prevent adipose accumulation, the bioassay comprising:

- (a) exposing a eukaryotic cell that expresses a protein encoded by a nucleotide having a sequence set forth in any one of SEQ.ID.NO. 1-279 to at least one compound whose ability to modulate the activity of the protein is sought to be determined; and thereafter
- (b) monitoring the cells for changes in activity, wherein change in activity identify a compound as a modulator of the human protein.

46. A compound identified by the method of any one of claims 32-45.

47. An isolated polynucleotide comprising

- a) a nucleotide sequence of SEQ ID NO:103;
- b) a nucleotide sequence coding for the polypeptide of SEQ.ID.NO. 603;
- c) a nucleotide sequence that has at least 91% identity over its entire length to a nucleotide sequence encoding the sFRP-5 polypeptide of SEQ ID NO:603 said identity being over the entire region encoding SEQ ID NO:603; or
- d) a nucleotide sequence complementary to the isolated nucleic acid molecule.

48. The isolated polynucleotide of claim 47 wherein expression of said gene upregulates its own expression in an autocrine fashion in adipocytes.

49. The isolated polynucleotide of claim 47 or 48 comprising a nucleotide sequence that is at least 91% identical with SEQ ID NO:103, said identity being over the entire length of SEQ ID NO:103.

50. The isolated polynucleotide of claim 47 or 48 comprising the nucleotide sequence of SEQ ID NO:103.

51. An isolated polynucleotide comprising a nucleotide sequence which, by virtue of redundancy of the genetic code, encodes for the amino acid of SEQ ID NO:603.

52. The polynucleotide of any one of claims 47-51 which is DNA or RNA.

53. The isolated polynucleotide of any one of claims 47-52, further comprising an expression system that is capable of transcribing the nucleic acid sequence and producing the corresponding amino acid sequence.

54. A host cell comprising a polynucleotide sequence of as defined in any one of claims 47-53.

55. The host cell of claim 54, wherein the polynucleotide sequence is stably incorporated into the genome of the host cell.

56. A process for producing an sFRP-5 polypeptide comprising culturing a host of claim 54 or 55 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.

57. A process for producing a cell which produces an sFRP-5 polypeptide comprising transforming or transfecting a host cell with the polynucleotide of claim 53 such that the host cell, under appropriate culture conditions, produces an sFRP-5 polypeptide.

58. An sFRP-5 polypeptide comprising an amino acid sequence which is at least 91% identical to the amino acid sequence of SEQ.ID.NO:603 over its entire length.

59. The polypeptide of claim 58 which comprises the amino acid sequence of SEQ ID NO:603.

60. An antibody immunospecific for the sFRP-5 polypeptide of claim 58.

61. A method for the treatment of a subject in need of enhanced activity or expression of the sFRP-5 polypeptide of claim 58 comprising:

(a) administering to the subject a therapeutically effective amount of an agonist to the polypeptide; and/or (b) administering to the subject an isolated polynucleotide comprising a nucleotide sequence that has at least 91% identity to a nucleotide sequence encoding the sFRP-5 polypeptide of SEQ.ID.NO.603 over its entire length, or a nucleotide sequence complementary to said nucleotide sequence in a form so as to effect production of such polypeptide in vivo; and/or (c) administering to a subject a therapeutically effective amount of the sFRP-5 polypeptide.

62. A method for the treatment of a subject in need of decreased activity or expression of the sFRP-5 polypeptide of claim 58 comprising:

(a) administering to the subject a therapeutically effective amount of an antagonist to said polypeptide; and/or (b) administering to the subject a nucleic acid molecule that inhibits the expression of the nucleotide sequence encoding said polypeptide; and/or (c) administering to the subject a therapeutically effective amount of a polypeptide that competes with said polypeptide for its ligand, substrate, or receptor.

63. A process for diagnosing a susceptibility to obesity in a subject related to expression or activity of the sFRP-5 polypeptide of claim 58 in a subject comprising: (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said sFRP-5 polypeptide in the genome of said subject; and/or (b) analyzing for the presence or amount of the sFRP-5 polypeptide expression in a sample derived from said subject.

64. A method for identifying compounds which antagonize or agonize the sFRP-5 polypeptide of claim 58 comprising:

(a) contacting a candidate compound(s) with cells which express the sFRP-5 polypeptide (or cell membrane expressing the sFRP-5 polypeptide or the sFRP-5 polypeptide or a fragment thereof bound to a solid matrix) or respond to the sFRP-5 polypeptide; and
(b) observing the binding, or stimulation or inhibition of a functional response; or comparing the ability of the cells (or cell membrane) which were contacted with the candidate compound(s) with the same cells which were not contacted for sFRP-5 polypeptide activity.

65. An agonist identified by the method of claim 64.

66. An antagonist identified by the method of claim 64.

67. A recombinant host cell produced by a method of claim 57 or a membrane thereof expressing an sFRP-5 polypeptide.

68. A method for screening for modulators of a target protein, wherein the target protein is sFRP-5 and comprises a sequence that has greater than 91% amino acid identity to SEQ ID NO:603 as measured using a sequence comparison algorithm, the method comprising the steps of

- a) contacting the target protein with a candidate agent at a first concentration and determining a level of activity of the target protein; and
- b) contacting the target protein with a candidate agent at a second concentration and determining a level of activity of the target protein; wherein a difference between the level of activity of the target protein contacted with the first concentration of the candidate agent and the level of activity of the target protein contacted with the second concentration of the candidate agent indicates that the candidate agent modulates the activity of the target protein.

69. The method of claim 68, wherein the screening occurs in a multi-well plate as part of a high-throughput screen.

70. The method of any one of claims 68-69, wherein the target protein has greater than 95% amino acid sequence identity to SEQ ID NO:603 as measured using a sequence comparison algorithm.

71. The method of any one of claims 68-70, wherein the target protein comprises an amino acid sequence of SEQ ID NO:603.

72. The method of claim 71, wherein the target protein has been isolated from an endogenous source.

73. The method of claim 71, wherein the target protein has been produced recombinantly.

74. The method of any one of claims 68-71, wherein said first concentration or said second concentration of the candidate agent is zero or at a level below detection.

75. The method of any one of claims 68-74, wherein the candidate agent is an agonist.

76. The method of any one of claims 68-74, wherein the candidate agent is an antagonist.

77. The method of any one of claims 68-74, wherein the candidate agent binds to the target protein.

78. The method of any one of claims 68-74, wherein the target protein is contacted with the candidate agent in vivo.

79. The method of any one of claims 68-74, wherein the target protein is contacted with the candidate agent in vitro.

80. The method of any one of claims 68-74, wherein the candidate agent is labeled.

81. A compound identified by the method of any one of claims 68-80.

82. An isolated polynucleotide comprising

- a) a nucleotide sequence of SEQ ID NO:278;
- b) a nucleotide sequence coding for the polypeptide of SEQ.ID.NO. 778;
- c) a nucleotide sequence that has at least 90% identity over its entire length to a nucleotide sequence encoding the npr3 polypeptide of SEQ ID NO:778 said identity being over the entire region encoding SEQ ID NO:778; or
- d) a nucleotide sequence complementary to the isolated nucleic acid molecule.

83. The isolated polynucleotide of claim 82 comprising a nucleotide sequence that is at least 90% identical with SEQ ID NO:278, said identity being over the entire length of SEQ ID NO:278.

84. The isolated polynucleotide of claim 82 comprising the nucleotide sequence of SEQ ID NO:278.

85. An isolated polynucleotide comprising a nucleotide sequence which, by virtue of redundancy of the genetic code, encodes for the amino acid of SEQ ID NO:778.

86. The polynucleotide of any one of claims 82-85 which is DNA or RNA.

87. The isolated polynucleotide of any one of claims 82-86, further comprising an expression system that is capable of transcribing the nucleic acid sequence and producing the corresponding amino acid sequence.

88. A host cell comprising a polynucleotide sequence of as defined in any one of claims 82-87.

89. The host cell of claim 88, wherein the polynucleotide sequence is stably incorporated into the genome of the host cell.

90. A process for producing an npr3 polypeptide comprising culturing a host of claim 88 or 89 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture.

91. A process for producing a cell which produces an npr3 polypeptide comprising transforming or transfecting a host cell with the polynucleotide of claim 87 such that the host cell, under appropriate culture conditions, produces an npr3 polypeptide.

92. An npr3 polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:778 over its entire length.

93. The polypeptide of claim 92 which comprises the amino acid sequence of SEQ ID NO:778.

94. An antibody immunospecific for the npr3 polypeptide of claim 92.

95. A method for the treatment of a subject in need of enhanced activity or expression of the npr3 polypeptide of claim 92 comprising:

(a) administering to the subject a therapeutically effective amount of an agonist to the polypeptide; and/or (b) administering to the subject an isolated polynucleotide comprising a nucleotide sequence that has at least 90% identity to a nucleotide sequence encoding the npr3 polypeptide of SEQ ID NO:778 over its entire length, or a nucleotide sequence complementary to said nucleotide sequence in a form so as to effect production of such polypeptide in vivo; and/or (c) administering to a subject a therapeutically effective amount of the npr3 polypeptide.

96. A method for the treatment of a subject in need of decreased activity or expression of the sFRP-5 polypeptide of claim 92 comprising:

(a) administering to the subject a therapeutically effective amount of an antagonist to said polypeptide; and/or (b) administering to the subject a nucleic acid molecule that inhibits the expression of the nucleotide sequence encoding said polypeptide; and/or (c) administering to the subject a therapeutically effective amount of a polypeptide that competes with said polypeptide for its ligand, substrate, or receptor.

97. A process for diagnosing a susceptibility to obesity in a subject related to expression or activity of the npr3 polypeptide of claim 92 in a subject comprising: (a) determining the presence or absence of a mutation in the nucleotide sequence encoding said npr3 polypeptide in the genome of said subject; and/or (b) analyzing for the presence or amount of the npr3 polypeptide expression in a sample derived from said subject.

98. A method for identifying compounds which antagonize or agonize the npr3 polypeptide of claim 92 comprising:

(a) contacting a candidate compound(s) with cells which express the npr3 polypeptide (or cell membrane expressing the npr3 polypeptide or a fragment thereof bound to a solid matrix); and

(b) observing the binding, or stimulation or inhibition of a functional response; or comparing the ability of the cells (or cell membrane) which were contacted with the candidate compound(s) with the same cells which were not contacted for npr3 polypeptide activity.

99. An agonist identified by the method of claim 98.

100. An antagonist identified by the method of claim 98.

101. A recombinant host cell produced by a method of claim 91 or a membrane thereof expressing an npr3 polypeptide.

102. A bioassay for identifying compounds which prevent adipose accumulation, the bioassay comprising:

(a) exposing a eukaryotic cell that expresses a heterologous npr3 receptor to at least one compound whose ability to modulate the activity of the receptor is sought to be determined; and thereafter

(b) monitoring the cells for changes in activity, wherein change in activity identify a compound as a modulator of human npr3 receptor.

103. A method for screening for compounds that modulate a target protein, wherein the target protein is npr3 and comprises a sequence that has greater than 90% amino acid identity to SEQ ID NO:778 as measured using a sequence comparison algorithm, the method comprising the steps of

a) contacting the target protein with a candidate agent at a first concentration and determining a level of activity of the target protein; and

b) contacting the target protein with a candidate agent at a second concentration and determining a level of activity of the target protein; wherein a difference between the level of activity of the target protein contacted with the first concentration of the candidate agent and the level of activity of the target protein contacted with the second concentration of the candidate agent indicates that the candidate agent modulates the activity of the target protein.

104. The method of claim 102 or 103, wherein the screening occurs in a multi-well plate as part of a high-throughput screen.

105. The method of any one of claims 102-104, wherein the target protein has greater than 95% amino acid sequence identity to SEQ ID NO:778 as measured using a sequence comparison algorithm.

106. The method of any one of claims 102-105, wherein the target protein comprises an amino acid sequence of SEQ ID NO:778.

107. The method of claim 106, wherein the target protein has been isolated from an endogenous source.

108. The method of claim 106, wherein the target protein has been produced recombinantly.

109. The method of any one of claims 102-106, wherein said first concentration or said second concentration of the candidate agent is zero or at a level below detection.

110. The method of any one of claims 102-109, wherein the candidate agent is an agonist.

111. The method of any one of claims 102-109, wherein the candidate agent is an antagonist.

112. The method of any one of claims 102-109, wherein the candidate agent binds to the target protein.

113. The method of any one of claims 102-109, wherein the target protein is contacted with the candidate agent in vivo.

114. The method of any one of claims 102-109, wherein the target protein is contacted with the candidate agent in vitro.

115. The method of any one of claims 102-109, wherein the candidate agent is labeled.

116. A compound identified by the method of any one of claims 102-115.